



**QUEEN'S
UNIVERSITY
BELFAST**

Do smoking and alcohol behaviours influence GI cancer survival?

McMenamin, Ú. C., McCain, S., & Kunzmann, A. T. (2017). Do smoking and alcohol behaviours influence GI cancer survival? *Best Practice & Research: Clinical Gastroenterology*. <https://doi.org/10.1016/j.bpg.2017.09.015>

Published in:

Best Practice & Research: Clinical Gastroenterology

Document Version:

Peer reviewed version

Queen's University Belfast - Research Portal:

[Link to publication record in Queen's University Belfast Research Portal](#)

Publisher rights

© 2017 Elsevier Ltd.

This manuscript is distributed under a Creative Commons Attribution-NonCommercial-NoDerivs License

(<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits distribution and reproduction for non-commercial purposes, provided the author and source are cited.

General rights

Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact openaccess@qub.ac.uk.

Do smoking and alcohol behaviours influence GI cancer survival?

Úna C McMenamin¹ PhD, Stephen McCain¹ MB, Andrew T Kunzmann¹ PhD

Contact information:

Email: u.mcmenamin@qub.ac.uk. Tel: 028 90971640

Email: smccain02@qub.ac.uk. Tel: 028 90971640

Email: a.kunzmann@qub.ac.uk. Tel: 028 90971640

Affiliations:

¹ Centre for Public Health, Institute of Clinical Sciences, Block B, Royal Victoria Hospital, Belfast, BT12 6BA

Corresponding author:

Dr Andrew T Kunzmann, Centre for Public Health, Institute of Clinical Sciences, Block B, Royal Victoria Hospital, Belfast, BT12 6BA. Email: a.kunzmann@qub.ac.uk

Word count: 7650

Conflict of Interest Statement:

None

Abstract

Little is known about the role of alcohol and smoking in GI cancer survival compared to GI cancer development.

We systematically reviewed the evidence for a role of smoking and alcohol in prognosis among GI cancer patients and inform whether smoking or alcohol cessation interventions or guidelines for GI cancer patients are likely to improve prognosis. A total of 84 relevant studies were identified.

Continued smokers, particularly heavy smokers, had worse prognosis than never smokers in most GI cancers. However, more evidence is needed to establish the likely impact of smoking cessation interventions amongst GI cancer patients.

Heavy alcohol drinkers had worse prognosis in oesophageal squamous cell carcinoma and hepatocellular carcinoma patients. Light alcohol consumption was not associated with worse prognosis from any GI cancer, though further studies are needed. UK guidelines for the general population recommending under 14 units (~7 drinks) per week may be sufficient for GI cancer patients, until further evidence is available.

Introduction

Most of the research on the role of alcohol and smoking in cancer has focussed on preventing cancer development. The role of lifestyle factors in prognosis following cancer diagnosis has not received the same attention though, meaning lifestyle recommendations for cancer patients are often based on evidence for cancer development [1]. For example, the World Cancer Research Fund (WCRF) consider alcohol to be a convincing risk factor for the development of various gastrointestinal (GI) cancers including colorectal, liver, oesophageal and gastric cancer, so recommend alcohol abstinence [2]. The WCRF also recommend that cancer survivors follow lifestyle guidelines for cancer risk [1] but have not directly assessed the role of alcohol in GI cancer survival. These recommendations are stricter than most national guidelines which allow light-moderate drinking but discourage heavy intakes [3].

The potentially important differences in the impact of cancer development and cancer survival mean a comprehensive evaluation of the role of lifestyle factors amongst the increasing number of cancer survivors is needed. Behaviour change Interventions targeted at cancer patients may also be more successful as cancer diagnoses could be considered a “teachable moment” [5], with cancer patients often motivated to make lifestyle changes, if given the correct support. Clinicians also often have a more detailed knowledge of the patient’s lifestyle behaviours which may enable them to identify high-risk individuals for behaviour change interventions.

This review took a systematic approach (Supplementary methods 1) to identify and summarise the evidence for a role of smoking and alcohol in prognosis among GI cancer patients and inform whether smoking or alcohol cessation interventions or guidelines for GI cancer patients are likely to improve prognosis.

Methodological considerations

The EMBASE electronic database (which includes MEDLINE references) were systematically searched for observational or interventional studies reporting results for the association between smoking or

alcohol and survival in GI cancer patients published in any language, until May 2016. The comprehensive terms for GI cancers, smoking and alcohol, study design and participants of interest are listed in Supplementary methods 1.

The search identified 5376 study articles. Titles and abstracts were screened, from which 313 potentially relevant articles were identified. Full-texts of these articles were then screened to assess eligibility: Reported results for the association(s) between smoking or alcohol behaviours and subsequent survival in GI cancer patients. A total of 84 relevant studies were included in the review.

Where possible, random effects meta-analyses were used to calculate pooled hazard ratios (HR) and 95% confidence intervals (CI) for the association between alcohol or smoking and survival in GI cancer patients.

We limited the review to studies reporting survival amongst cohorts of GI cancer patients, as cancer mortality outcomes amongst non-cancer cohorts may be affected by the lifestyle factors association with both cancer development and severity of cancer at diagnosis. Some studies have reported on overall survival, which accounts for deaths from any cause and may represent a more comprehensive impact of smoking and alcohol on cancer patients. Some studies presented results for cancer-specific survival, which only accounts for deaths attributed to cancer but may be more useful for understanding the biological mechanism through which smoking and alcohol influence cancer progression.

Unfortunately, to our knowledge, no randomised controlled trials have assessed the impact of smoking cessation or alcohol reduction interventions on survival amongst GI cancer patients.

Therefore, the review relies on observational evidence, which could be subject to confounding, making a focus on adjusted results necessary where possible.

Studies measuring smoking and alcohol after diagnosis may capture changes following diagnosis and better reflect the likely impact of interventions beginning after diagnosis. However, studies measuring smoking and alcohol prior to diagnosis may be less subject to reporting bias, short-term behaviour changes and selective recruitment to longer-term survivors. Therefore, each approach has its strengths, though selective recruitment may be a particular issue for studies attempting to measure smoking or alcohol after diagnosis of GI cancers with poorer survival.

In order to assess whether smoking cessation interventions are warranted we would ideally have results from studies comparing survival in patients who quit following diagnosis to patients who continued smoking. In absence of this we will examine whether patients who quit close to diagnosis have better survival profiles than continued smokers.

In terms of alcohol assessment it is important to distinguish between light-moderate, and heavier alcohol consumption as alcohol appears to have a j-shape relationship with risk of death in the general population [6]. It is also important to examine differences compared to lifetime never drinkers, to minimise reverse causality caused by patients with worse health or prognosis giving up drinking.

Colorectal cancer

Smoking and colorectal cancer survival

We identified 29 studies [7–35] that have provided estimates for the association between smoking behaviours and survival amongst cohorts of colorectal cancer patients from around the world (Supplementary table 1).

The evidence to date provides substantial evidence that smoking is associated with colorectal cancer prognosis. Consistent with a previous systematic review [36], we found that current smokers have poorer overall and cancer-specific survival than never smokers (n=11 studies [7–17], HR 1.39, 95% CI 1.21 to 1.60, Table 1; n=8 studies [13–20], HR 1.35, 95% CI 1.16 to 1.58, Figure 1, respectively). A

dose-response was also apparent, as heavier smokers had poorer survival than never smokers (n=5 studies [11–14,21], HR 1.52, 95% CI 1.31 to 1.77); whereas the difference in survival in lighter smokers compared to never smokers was smaller and not statistically significant (n=5 studies [11–14,21], HR 1.13, 95% CI: 0.88 to 1.45, Table 1). The impact of smoking on survival may begin shortly after diagnosis or surgery [22,23]. Therefore, prognosis of colorectal cancer patients appears to differ based on smoking status and intensity, with heavy current smokers having the poorest prognosis.

The results for former smokers are less consistent, as the results indicate a more modest, non-statistically significant increase in risk of death from any cause (n=9 studies [8–16], HR 1.10, 95% CI: 0.96-1.27, Table 1) but little or no increase in risk of death from colorectal cancer (n=6 studies [13–16,18–20], HR 1.03, 95% CI 0.96 to 1.10) (Figure 1). However, the result for overall survival was strengthened when limited to studies which adjusted for tumour stage (n=7 studies [8,10–12,14–16], HR 1.20, 1.10 to 1.30). The excess risk of death compared to never smokers tended to be smaller in former smokers who had quit many years prior to diagnosis (n=4 studies [12–15], HR 1.18, 95% CI 1.01-1.39, Table 1), than former smokers who quit closer to diagnosis (HR 1.40 [12–15], 95% CI 1.22-1.61, Table 1). Nevertheless this excess risk (compared to never smokers) still tends to be smaller in recent quitters than in current smokers (HR 1.72 95% CI 1.49 to 1.99) in the same studies [12–15] indicating smoking cessation closer to diagnosis may still confer a survival benefit. However, the broad boundaries for the more recent quitter estimates (<10 or even <20 years prior to diagnosis) used in these studies makes it difficult to adequately estimate the likely survival benefit for patients who stop smoking following a diagnosis of colorectal cancer.

Unfortunately, there is limited evidence directly assessing the likely impact of smoking cessation on prognosis by comparing continued smokers to patients who quit following diagnosis. An analysis within the Shanghai Cohort study did find that colorectal cancer patients who quit smoking within the first year after diagnosis had better subsequent survival than patients who continued to smoke

[24]. However, other studies did not find a difference between continued smokers and recent quitters [13,21,37], though numbers of recent quitters were small.

In summary, whilst there is substantial evidence that current smokers, particularly heavy smokers, have worse survival than never smokers, however more large-scale studies comparing survival in recent quitters to continued smokers would be useful to advocate targeted smoking cessation interventions in colorectal cancer patients.

Alcohol & colorectal cancer survival

We identified 15 studies assessing the association between alcohol intakes and survival in colorectal cancer patients [8–10,13,15,38–47] from around the world (Supplementary table 1). Many of the studies identified did not adequately separate light, moderate and heavy drinkers [41–43,45].

The results suggest that light, or light-moderate, alcohol consumption may be associated with better survival than complete abstention in patients with colorectal cancer. Nickelsen et al [22] found that 30-day mortality following surgery for colorectal cancer was better amongst light-moderate drinkers than non-drinkers. Long-term survival may also be improved, as pooled analyses suggested light or light-moderate drinkers had better overall survival (n=7 studies [9,10,13,15,38,46,47], HR 0.85, 95% CI: 0.77 to 0.94, Table 1) and colorectal cancer specific survival (n=5 studies [13,15,38,46,47], HR 0.82, 95% CI: 0.67-1.00, Figure 2) than non- or never drinkers. The results seem robust to differences in assessment timing, as no major differences were apparent between studies using pre-diagnostic measures and post-diagnostic measures. However, reverse causality is hard to rule out as the results for colorectal cancer specific survival from two studies using lifetime never drinkers as comparison are less consistent [46,47] and may warrant additional study. Therefore, it appears that colorectal cancer patients who consume light amounts of alcohol have better survival profiles than non-drinkers. This result should be interpreted cautiously and should not be taken to suggest non-drinkers begin drinking after diagnosis but indicates that colorectal cancer patients may not need to abstain from light drinking.

The evidence for the impact of heavier alcohol consumption on survival in colorectal cancer patients is less clear. No major differences in survival in heavier drinkers were observed when compared to non/never drinkers (n=6 studies, HR 0.92, 95% CI 0.84-1.01). However, a J-shape association was noted in some studies, with heavier drinkers having poorer survival when compared to light drinkers [8,39,46], though this was not reflected in other studies as the excess risk compared to never drinkers was similar in heavy drinkers and light drinkers [9,10,13,15,38,47]. More studies comparing heavier drinkers to light drinkers are needed to assess whether alcohol reduction interventions would benefit colorectal cancer patients who drink heavily. Timing may also be important as avoiding heavy alcohol consumption during chemotherapy may be warranted due to potential interactions in the liver [48].

Analyses by type of alcohol consumed indicate that light-moderate wine consumption is associated with improved survival compared to never or non-drinking (n=4 studies [13,43,44,46], HR 0.85, 95% CI 0.77 to 0.94, Figure 3). Similar but not statistically significant improvements apparent for heavier wine drinkers (n=3 studies [13,43,44], HR 0.73, 95% CI 0.52 to 1.01). No reductions were apparent for either light or heavier consumption of either beer or liquor in any of the studies to date (Figure 3).

In summary, the evidence to date suggests that most national guidelines for the general population, which discourage heavy drinking [4,3], may be sufficient for colorectal cancer patients and WCRF guidelines recommending complete abstinence [1] may be too strict. Further prognostic studies which adequately distinguish between lighter and heavier alcohol consumption, ideally using lifetime never drinkers as a comparison group, would help inform whether new guidelines or alcohol reduction interventions are warranted.

Oesophageal cancer

Smoking and survival in oesophageal cancer patients

We identified a total of 20 studies [9,49–65] which investigated the impact of smoking on survival in patients diagnosed with oesophageal cancer (Supplementary table 2). Most studies were single-centred and focused on patients with oesophageal squamous cell carcinoma.

There was little evidence of an association between current or former smoking status and survival in pooled analyses from all oesophageal cancers (Table 1). However, when restricted to patients with oesophageal squamous cell carcinoma, poorer survival was indicated for current as well as former smokers compared to never-smokers (n=2 studies [58,59], HR 1.41, 95% CI 0.96, 2.09; n=2 studies [58,59], HR 1.44, 95% CI 0.81, 2.55), which appeared to be driven by an Australian population-based study of 301 patients [59]. Although a clear dose-response relationship was not evident, there was evidence that patients who reported heavy smoking experienced a significantly shorter survival compared to moderate or light smokers and again this was restricted to patients with oesophageal squamous cell carcinoma patients (heavy n=2 studies [56,59], HR 1.46, 95% CI 1.05, 2.03). Only one study investigated the impact of smoking on cancer-specific mortality and observed no significant association with former smoking but there was somewhat of a dose-response relationship seen moderate (HR 1.40, 95% CI 0.74-1.83) and heavy (HR 1.79, 95% CI 1.13-2.30) smoking compared to never smoking [51]. There was little evidence of any associations between smoking exposure and survival in oesophageal adenocarcinoma patients. Spreafico et al. [57] found no association with survival for every unit increase in pack-years smoked prior to oesophageal adenocarcinoma diagnosis (adjusted HR 1.01, 95% CI 1.00-1.01).

In summary, patients diagnosed with oesophageal squamous cell carcinoma who had a history of smoking, particularly current smokers, experienced a shorter survival after diagnosis, which corroborates the findings from a previous systematic review [66]. Further studies comparing current to former smokers (ideally recent quitters) are required to determine whether smoking cessation

interventions are warranted. No association was evident for patients diagnosed with oesophageal adenocarcinoma but the paucity of available data limited the interpretation of these findings.

Additional studies in Western countries, where oesophageal adenocarcinoma rates are at their highest [67], are particularly necessary considering the markedly increasing rates in incidence [68]

Alcohol and survival in oesophageal cancer patients

A total of 15 studies [9,51,53,55,56,58–61,63,65,69–72], mostly in Asian populations, were identified that provided estimates to examine associations between alcohol consumption and risk of death after oesophageal cancer (Supplementary table 2). Few studies distinguish between light, moderate and heavy drinkers.

Overall, there was a significantly worse survival observed for patients who reported to have ever consumed alcohol (n=9 studies[53,55,61,63,65,69,71,72] , HR 1.23, 95% CI 1.10,1.37), which was concentrated specifically among studies of oesophageal squamous cell carcinoma patients. Only one study assessed the impact of current and former alcohol use and found a significant increase in mortality for current users (HR 3.01, 95% CI 1.64, 5.53) which was slightly attenuated in former users (HR 2.34, 95% CI 1.14, 4.82). Three studies [58,59,72] examined dose-response relationships with alcohol consumption in oesophageal cancer patients and although non-significant, overall there were indications of increased risk of death for moderate (n=5 studies [58–60,72], HR 1.26, 95% CI 0.92, 1.73) and heavy users (n=8 studies [9,56,58–60,70,72], HR 1.23, 95% CI 0.94, 1.61). Significant increases for light, moderate and heavy alcohol intakes were seen in a population-based study of 301 oesophageal squamous cell carcinoma patients [59]. Too few studies have examined the association with cancer-specific survival for firm conclusions to be made [51]. In oesophageal adenocarcinoma patients, there was little evidence of associations with survival in three population-based studies [58,60,61]. However, a suggestion of an increase in mortality risk was noted for moderate versus light or never drinkers (n=2 studies [58,60], HR 1.34, 95% CI 0.95, 1.89), primarily due to the findings from Thrift et al [60].

In summary, the findings suggest that alcohol drinking affects prognosis in oesophageal squamous cell carcinoma patients, which is in agreement with a previous systematic review [66]. Former users of alcohol experienced a better survival in comparison to current alcohol users, which suggests that alcohol reduction interventions at diagnosis may be of benefit but large-scale studies are required to confirm these findings. There was a notable absence of studies in patients with oesophageal adenocarcinoma, and the relationship between moderate alcohol consumption and survival outcomes needs to be further elucidated.

Gastric cancer

Smoking and survival in gastric cancer patients

A total of 10 studies [9,24,55,58,61,73–78] which evaluated the influence of smoking on overall survival in gastric cancer patients were identified (Supplementary table 2). Five studies were population-based and smoking exposure was primarily reported for the period prior to cancer diagnosis. There was variation in the prognostic factors adjusted for across studies (Table 1).

There was evidence of a significant increase in mortality amongst gastric patients who reported ever smoking compared to never smoking (n=7 studies [53,55,61,74,76,78], HR 1.25, 95% CI 1.02 to 1.55). The evidence suggested that current but not former smoking was positively associated with risk of death (n=6 studies [9,24,58,73,75,76], HR 1.39, 95% CI 0.96 to 2.01; n=5 studies [9,58,73,75,76], HR 1.05, 95% CI 0.76 to 1.45, respectively). The lack of an observed relationship for former smoking may be due to the protective association reported by Park et al. [9] however, this study lacked information on cancer stage. There was a modest dose-response relationship observed with increasing smoking exposure from moderate to heavy (moderate n=6 studies [9,58,73,75–77], HR 1.13, 95% CI 0.81 to 1.58; heavy n=2 studies [75,76], HR 1.97, 95% CI 1.08 to 3.59). Only one study [24] examined the influence of post-diagnosis smoking and reported a worse survival in patients who were smokers compared to those who were non-smokers in the Shanghai Cohort study (HR 1.76, 95% CI 1.11 to 2.79). In addition, when analysis was restricted to patients who were current smokers

at diagnosis, there was a suggestion of an increase in mortality risk in patients who continued to smoke after diagnosis relative to those who quit (HR1.36, 95% CI 0.70 to 2.67), which may imply that smoking cessation interventions would be of benefit.

In summary, smoking prior to cancer diagnosis was associated with a worse overall survival, especially for patients who reported heavy exposure. Further studies are necessary to determine if smoking cessation after gastric cancer diagnosis leads to better survival. Future studies should aim to collect detailed information on the timing and intensity of smoking exposure and aim to standardise measurement categories.

Alcohol and survival in gastric cancer patients

There is probable evidence that alcohol and specifically heavy alcohol consumption increases the risk gastric cancer (WCRF). We identified six studies [55,58,61,73,75,76]with available risk estimates for inclusion (Supplementary table 2).

No association was observed in ever consumers of alcohol compared to never consumers and similarly, there was little evidence of associations for current (n=3 studies [73,75,76], HR 1.05, 95% CI 0.80, 1.37) or former users (n=3 studies [73,75,76], HR 1.02, 95% CI 0.65, 1.60) compared to never users. In pooled analysis, there was no dose-response associations evident among studies that categorised alcohol intakes into light, moderate or heavy. Few studies separated results by gastric cancer type or location [58,61,75] but there were little differences observed in results in comparison to studies of gastric cancer patients combined.

In summary, alcohol consumption was not associated with survival in gastric cancer patients however; the lack of studies identified limits our interpretation. Moreover, most studies captured information on alcohol consumption at one time-point so there may be a risk that previous (or current) heavy consumers of alcohol falsely report that they are non-users of alcohol. Future studies should aim to collect detailed information on the timing of alcohol intake in relation to cancer diagnosis, as well as information on the types of alcohol consumed.

Liver cancer

Smoking and survival in liver cancer patients

Only 3 studies [79–81] identified assessed the association between smoking and survival amongst liver cancer patients (Supplementary table 3).

In hepatocellular carcinoma patients with viral hepatitis, Shih et al [81] found that current smokers had worse liver cancer specific survival than never smokers (HR 1.25, 95% CI 1.09–1.44) and Holly et al [80] found that current smokers had worse overall survival than non-smokers (HR 2.41, 95% CI 1.28-4.55). In contrast in hepatocellular carcinoma patients without viral hepatitis, neither Shih et al [81] nor Kolly et al [80] found any association between smoking and survival outcomes. However, Kai et al [79] did find that current smokers had poorer overall and liver cancer specific survival compared to never smokers and former smokers, respectively, in a cohort of hepatocellular carcinoma patients without hepatitis. Importantly all results adjusted for important confounders such as age, obesity, tumour size/stage and alcohol history, suggesting the results are unlikely to be substantially influenced by confounding. Therefore, whilst the evidence indicates that current smoking is associated with worse prognosis in hepatocellular carcinoma patients with viral hepatitis, the evidence is less clear in patients without viral hepatitis. The limited number of studies for both types of hepatocellular carcinoma means that more observational studies are needed to clarify whether smoking cessation intervention trials could be warranted.

Alcohol and survival in liver cancer patients

Nine studies [79–87] assessed the association between alcohol consumption and survival in hepatocellular carcinoma patients (Supplementary table 3). Many of these studies used measures of historical heavy alcohol consumption rather than current alcohol use. Findings vary considerably between studies, though most studies found no association [80,82,84], some found an association with worse survival [85], and one found an association with improved survival [86] in historical heavy

drinkers compared to non-heavy drinkers. This could be due to differences in definition of heavy alcohol use and the length of the reference period over which alcohol use was assessed.

Only one study, Shih et al [81], adequately distinguished between never, light and heavy drinkers. Shih et al found that current drinkers had worse liver cancer specific survival, though when intakes were separated by daily or cumulative intakes, only heavy intakes ($>46.2\text{g/d}$; $>2744.6\text{ gram-years}$) were associated with worse survival. The pattern of results was similar between patients with and without viral hepatitis. Therefore, the existing evidence indicates that heavy but not light, alcohol consumption is associated with worse survival. The results also indicated that patients who quit drinking prior to diagnosis had better survival than continuing drinkers, though the result was only statistically significant for patients who quit 10 or more years before diagnosis. More well designed observational studies separating light and heavy drinkers are needed before trials assessing evidence-based alcohol reduction interventions are warranted.

Pancreatic cancer

Smoking and survival in pancreatic cancer patients

We identified nine studies with available risk estimates for inclusion in the review [88–96] (Supplementary table 4). Most studies were conducted in the United States. Only two were population-based [89,92]. Information on smoking status was primarily obtained from hospital medical records at cancer diagnosis.

Overall, ever smoking was associated with a significant 20% increase risk of death compared to never smoking ($n=5$ studies [88,89,93,94,96], HR 1.20, 95% CI 1.05, 1.37) with similar findings observed for current smokers compared to never smokers ($n=5$ studies [90–92,95,96], HR 1.19, 95% CI 0.97, 1.46), albeit non-significant. Former smokers experienced a 14% significant increase in mortality risk compared to never smokers ($n=5$ studies [90–92,95,96], HR 1.14, 95% CI 1.01, 1.30) and a marked worse survival was demonstrated in patients who recently quit smoking in the 15

years preceding cancer diagnosis (n=2 studies [92,96], HR 1.42 95% CI 1.16, 1.74). In contrast, there was little evidence that long-term quitters (>15 years before diagnosis) experienced an increase in mortality (n=2 studies [92,96], HR 1.11, 95% CI 0.85, 1.44). Pelucchi et al. [96] was the only study to investigate smoking dose-response relationships and found significant increases in mortality in more moderate and heavy smokers compared to light smokers (e.g. ≥ 20 cigarettes per day: HR 1.57, 95% CI 1.26, 1.96, ≥ 30 years smoking: HR 1.49, 95% CI 1.22, 1.83 and > 20 pack-years HR 1.49, 95% CI 1.21, 1.83).

Overall, these results provide support for a detrimental role of tobacco smoking on survival after pancreatic cancer. Considering the particularly poor survival in patients who recently quit smoking prior to diagnosis, these findings support continuation of smoking cessation strategies in the general population, prior to the development of pancreatic cancer.

Alcohol and survival in pancreatic cancer patients

We identified only two studies that investigated the association between alcohol intake and overall survival in pancreatic cancer patients [93,96] (Supplementary table 4). Both studies were hospital-based and only one adjusted for prognostic factors (including age and sex).

Pelucchi et al. [96] did not show any significant associations between patients who reported consuming < 3 drinks per day (HR 0.88, 95% CI 0.71, 1.09) or ≥ 3 drinks per day (HR 0.96, 95% CI 0.76, 1.21) compared to non-drinkers. Wang et al. [93] also failed to show a significant association between patients who reported ever consuming alcohol compared to never drinkers at diagnosis (HR 1.16, 95% CI 0.91–1.47).

These findings do not suggest that alcohol impacts upon survival in pancreatic cancer patients but only two studies were identified. Population-based studies, with sufficient information on the amount and type of alcohol consumed, as well as the timing of alcohol exposure are required to further investigate the relationship between alcohol use and pancreatic cancer prognosis.

Practice points: Alcohol

- Alcohol is an established risk factor for the development of most GI cancers (except oesophageal adenocarcinoma)
- Less is known about the role of alcohol in GI cancer prognosis
- Heavy alcohol intakes were linked with worse prognosis in oesophageal squamous cell carcinoma and hepatocellular carcinoma
- Light alcohol consumption were not associated with worse prognosis from any GI cancer

Research agenda: Alcohol

- More prognostic studies separating light, moderate and heavy alcohol intakes are needed amongst cohorts of GI cancer patients, particularly for oesophageal adenocarcinoma, liver cancer and pancreatic cancer
- Alcohol reduction intervention trials may be warranted in oesophageal squamous cell carcinoma patients

Practice points: Smoking

- Smoking is a risk factor for various GI cancers, especially oesophageal squamous cell carcinoma
- Heavy smoking is linked with worse prognosis for most GI cancers, except oesophageal adenocarcinoma
- Some of the association between smoking and prognosis remained amongst former smokers

Research agenda: Smoking

- More studies comparing survival in patients who quit following diagnosis to continued smokers are needed
- Prognostic studies are needed in oesophageal adenocarcinoma and hepatocellular carcinoma patients

References

- [1] World Cancer Research Fund. Cancer survivors | World Cancer Research Fund International
n.d. <http://www.wcrf.org/int/research-we-fund/cancer-prevention-recommendations/cancer-survivors> (accessed July 24, 2017).
- [2] World Cancer Research Fund. Global status report on alcohol and health 2014. Geneva: 2014.
- [3] Kalinowski A, Humphreys K. Governmental standard drink definitions and low-risk alcohol consumption guidelines in 37 countries. Addiction 2016;111:1293–8.
- [4] Department of Health. UK Chief Medical Officers' Alcohol Guidelines Review: Summary of the proposed new guidelines 2015:7.
- [5] Karvinen K, Bruner B, Truant T. The Teachable Moment After Cancer Diagnosis: Perceptions From Oncology Nurses. Oncol Nurs Forum 2015;42:602–9.
- [6] Ferrari P, Licaj I, Muller DC, Kragh Andersen P, Johansson M, Boeing H, et al. Lifetime alcohol use and overall and cause-specific mortality in the European Prospective Investigation into Cancer and nutrition (EPIC) study. BMJ Open 2014;4:e005245.
- [7] Raja Ali RA, Dooley C, Comber H, Newell J, Egan LJ. Clinical Features, Treatment, and Survival of Patients With Colorectal Cancer With or Without Inflammatory Bowel Disease. Clin Gastroenterol Hepatol 2011;9:584–9.
- [8] Aarts MJ, Kamphuis CBM, Louwman MJ, Coebergh JWW, Mackenbach JP, van Lenthe FJ. Educational inequalities in cancer survival: a role for comorbidities and health behaviours? J Epidemiol Community Heal 2013;67:365–73.
- [9] Park SM, Lim MK, Shin SA, Yun YH. Impact of prediagnosis smoking, alcohol, obesity, and insulin resistance on survival in male cancer patients: National Health Insurance Corporation

Study. J Clin Oncol 2006;24:5017–24.

- [10] Tamakoshi A, Nakamura K, Ukawa S, Okada E, Hirata M, Nagai A, et al. Characteristics and prognosis of Japanese colorectal cancer patients: The BioBank Japan Project. J Epidemiol 2017;27:S36–42.
- [11] McCleary NJ, Niedzwiecki D, Hollis D, Saltz LB, Schaefer P, Whittom R, et al. Impact of smoking on patients with stage iii colon cancer: Results from cancer and leukemia group B 89803. Cancer 2010;116:957–66.
- [12] Zhu Y, Yang SR, Wang PP, Savas S, Wish T, Zhao J, et al. Influence of pre-diagnostic cigarette smoking on colorectal cancer survival: overall and by tumour molecular phenotype. Br J Cancer 2014;110:1359–66.
- [13] Phipps AI, Baron J, Newcomb PA. Prediagnostic smoking history, alcohol consumption, and colorectal cancer survival: The Seattle Colon Cancer Family Registry. Cancer 2011;117:4948–57.
- [14] Yang B, Jacobs EJ, Gapstur SM, Stevens V, Campbell PT. Active smoking and mortality among colorectal cancer survivors: The cancer prevention study II nutrition cohort. J Clin Oncol 2015;33:885–93.
- [15] Pelsler C, Arem H, Pfeiffer RM, Elena JW, Alfano CM, Hollenbeck AR, et al. Prediagnostic lifestyle factors and survival after colon and rectal cancer diagnosis in the National Institutes of Health (NIH)-AARP Diet and Health Study. Cancer 2014;120:1540–7.
- [16] Boyle T, Fritschi L, Platell C, Heyworth J. Lifestyle factors associated with survival after colorectal cancer diagnosis. Br J Cancer 2013;109:814–22.
- [17] Warren GW, Kasza KA, Reid ME, Cummings KM, Marshall JR. Smoking at diagnosis and survival in cancer patients. Int J Cancer 2013;132:401–10.

- [18] Dianatinasab M, Ghaem H, Rezaianzadeh A, Hosseini SV, Khazraei H. Colorectal cancer mortality in Shiraz, Iran. Asian Pacific J Cancer Prev 2016;17:4101–5.
- [19] Sharp L, McDevitt J, Brown C, Carsin A-E, Comber H. Association between smoking at diagnosis and cause-specific survival in patients with rectal cancer: Results from a population-based analysis of 10,794 cases. Cancer 2017;123:2543–50.
- [20] Sharp L, McDevitt J, Brown C, Comber H. Smoking at diagnosis significantly decreases 5-year cancer-specific survival in a population-based cohort of 18 166 colon cancer patients. Aliment Pharmacol Ther 2017;45:788–800.
- [21] Walter V, Jansen L, Hoffmeister M, Ulrich A, Chang-Claude J, Brenner H. Smoking and survival of colorectal cancer patients: Population-based study from Germany. Int J Cancer 2015;137:1433–45.
- [22] Nickelsen TN, Jørgensen T, Kronborg O. Lifestyle and 30-day complications to surgery for colorectal cancer. Acta Oncol 2005;44:218–23.
- [23] Sharma A, Deeb A-P, Iannuzzi JC, Rickles AS, Monson JRT, Fleming FJ. Tobacco Smoking and Postoperative Outcomes After Colorectal Surgery. Ann Surg 2013;258:296–300.
- [24] Tao L, Wang R, Gao YT, Yuan JM. Impact of postdiagnosis smoking on long-term survival of cancer patients: The Shanghai Cohort Study. Cancer Epidemiol Biomarkers Prev 2013;22:2404–11.
- [25] Richards CH, Leitch EF, Horgan PG, Anderson JH, McKee RF, McMillan DC. The relationship between patient physiology, the systemic inflammatory response and survival in patients undergoing curative resection of colorectal cancer. Br J Cancer 2010;103:1356–61.
- [26] Mathis KL, Green E, Sargent DJ, Boardman L, Limburg PJ, Thibodeau SN, et al. Smoking adversely affects colon cancer survival and relapse rates. Gastroenterol. Conf. Dig. Dis. Week, Orlando: 2013, p. S1117.

- [27] Ahmadi A, Mosavi-Jarrahi A, Pourhoseingholi MA. Mortality determinants in colorectal cancer patients at different grades: a prospective, cohort study in Iran. Asian Pac J Cancer Prev 2015;16:1069–72.
- [28] Rasouli MA, Moradi G, Roshani D, Nikkhoo B, Ghaderi E, Ghaytasi B. Prognostic factors and survival of colorectal cancer in Kurdistan province, Iran 2014:1–7.
- [29] Munro AJ, Bentley AHM, Ackland C, Boyle PJ. Smoking Compromises Cause-specific Survival in Patients with Operable Colorectal Cancer. Clin Oncol 2006;18:436–40.
- [30] Kato I, Dyson G, Kim H, Severson K. Differential effects of patient-related factors on the outcome of radiation therapy for rectal cancer. J Radiat Oncol 2016;5:279–86.
- [31] Vincenzi B, Santini D, Loupakis F, Addeo R, Rojas Llimpe FL, Baldi GG, et al. Cigarettes smoking habit may reduce benefit from cetuximab-based treatment in advanced colorectal cancer patients. Expert Opin Biol Ther 2009;9:945–9.
- [32] Phipps AI, Shi Q, Newcomb PA, Nelson GD, Sargent DJ, Alberts SR, et al. Associations between cigarette smoking status and colon cancer prognosis among participants in North Central Cancer Treatment Group Phase III Trial N0147. J Clin Oncol 2013;31:2016–23.
- [33] Diamantis N, Xynos ID, Amptulah S, Karadima M, Skopelitis H, Tsavaris N. Prognostic significance of smoking in addition to established risk factors in patients with Dukes B and C colorectal cancer: A retrospective analysis. J BUON 2013;18:105–15.
- [34] Ottaiano A, Nappi A, Tafuto S, Nasti G, De Divitiis C, Romano C, et al. Diabetes and Body Mass Index Are Associated with Neuropathy and Prognosis in Colon Cancer Patients Treated with Capecitabine and Oxaliplatin Adjuvant Chemotherapy. Oncol 2016;90:36–42.
- [35] Jadallah F, McCall JL, van Rij AM. Recurrence and survival after potentially curative surgery for colorectal cancer. N Z Med J 1999;112:248–50.

- [36] Walter V, Jansen L, Hoffmeister M, Brenner H. Smoking and survival of colorectal cancer patients: systematic review and meta-analysis. Ann Oncol 2014;25:1517–25.
- [37] Warren GW, Kasza KA, Reid ME, Cummings KM, Marshall JR. Smoking at diagnosis and survival in cancer patients. Int J Cancer 2013;132:401–10.
- [38] Lochhead P, Nishihara R, Qian ZR, Mima K, Cao Y, Sukawa Y, et al. Postdiagnostic intake of one-carbon nutrients and alcohol in relation to colorectal cancer survival. Am J Clin Nutr 2015;102:1134–41.
- [39] Fung TT, Kashambwa R, Sato K, Chiuve SE, Fuchs CS, Wu K, et al. Post diagnosis diet quality and colorectal cancer survival in women. PLoS One 2014;9:1–13.
- [40] Romaguera D, Ward H, Wark PA, Vergnaud A-C, Peeters PH, van Gils CH, et al. Pre-diagnostic concordance with the WCRF/AICR guidelines and survival in European colorectal cancer patients: a cohort study. BMC Med 2015;13:107.
- [41] Asghari-Jafarabadi M, Hajizadeh E, Kazemnejad a, Fatemi SR. Site-specific evaluation of prognostic factors on survival in Iranian colorectal cancer patients: a competing risks survival analysis. Asian Pac J Cancer Prev 2009;10:815–21.
- [42] Mehrabani D, Almasi-hashiani A, Moshfeghi K, Khedmati E. Survival Rate and its Predictors in Colorectal Cancer Patients , Southern Iran 2012;12:1072–7.
- [43] Phipps AI, Shi Q, Limburg PJ, Nelson GD, Sargent DJ, Sinicrope FA, et al. Alcohol consumption and colon cancer prognosis among participants in north central cancer treatment group phase III trial N0147. Int J Cancer 2016;139:986–95.
- [44] Phipps AI, Robinson JR, Campbell PT, Win AK, Figueiredo JC, Lindor NM, et al. Prediagnostic alcohol consumption and colorectal cancer survival: The Colon Cancer Family Registry. Cancer 2017;123:1035–43.

- [45] Zell JA, McEligot AJ, iogas A, Holcombe RF, Anton-Culver H. Differential effects of wine consumption on colorectal cancer outcomes based on family history of the disease. Nutr Cancer 2007;59:36–45.
- [46] Walter V, Jansen L, Ulrich A, Roth W, Bläker H, Chang-Claude J, et al. Alcohol consumption and survival of colorectal cancer patients: a population-based study from Germany. Am J Clin Nutr 2016;103:1497–506.
- [47] Yang B, Gapstur SM, Newton CC, Jacobs EJ, Campbell PT. Alcohol intake and mortality among survivors of colorectal cancer: The Cancer Prevention Study II Nutrition Cohort. Cancer 2017;123:2006–13.
- [48] Cancer Research UK. Alcohol and chemotherapy | Cancer in general | Cancer Research UK n.d. <http://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/chemotherapy/living-with/alcohol> (accessed July 24, 2017).
- [49] Aghcheli K, Marjani HA, Nasrollahzadeh D, Islami F, Shakeri R, Sotoudeh M, et al. Prognostic factors for esophageal squamous cell Carcinoma-A Population-Based study in Golestan province, Iran, a high incidence area. PLoS One 2011;6.
- [50] Guo W, Xiao H-L, Ma Z, Liu H-J, Wang Y-J, Mei L-Y, et al. Should stage T2 esophageal squamous cell carcinoma be subclassified? Ann Surg Oncol 2014;21:2540–5.
- [51] Jing C, Huang Z, Duan Y, Xiao X, Zhang R, Jiang J. Folate intake, methylenetetrahydrofolate reductase polymorphisms in association with the prognosis of esophageal squamous cell carcinoma. Asian Pac J Cancer Prev 2012;13:647–51.
- [52] Lin C, Chang S, Wei Y, Wang L, Hsu W. Prognostic Variables in Thoracic Esophageal. Ats 2009;87:1056–65.
- [53] Okada E, Ukawa S, Nakamura K, Hirata M, Nagai A, Matsuda K, et al. Demographic and lifestyle factors and survival among patients with esophageal and gastric cancer: The Biobank

Japan Project. J Epidemiol 2017;27:S29–35.

- [54] Raymond DP, Seder CW, Wright CD, Magee MJ, Kosinski AS, Cassivi SD, et al. Predictors of Major Morbidity or Mortality after Resection for Esophageal Cancer: A Society of Thoracic Surgeons General Thoracic Surgery Database Risk Adjustment Model. Ann Thorac Surg 2016;102:207–14.
- [55] Samadi F, Babaei M, Yazdanbod A, Fallah M, Nouraie M, Nasrollahzadeh D, et al. Survival rate of gastric and esophageal cancers in Ardabil province, North-West of Iran. Arch Iran Med 2007;10:32–7.
- [56] Shitara K, Matsuo K, Hatooka S, Ura T, Takahari D, Yokota T, et al. Heavy smoking history interacts with chemoradiotherapy for esophageal cancer prognosis: A retrospective study. Cancer Sci 2010;101:1001–6.
- [57] Spreafico A, Coate L, Zhai R, Xu W, Chen ZF, Chen Z, et al. Early adulthood body mass index, cumulative smoking, and esophageal adenocarcinoma survival. Cancer Epidemiol 2017;47:28–34.
- [58] Sundelöf M, Lagergren J, Ye W. Patient demographics and lifestyle factors influencing long-term survival of oesophageal cancer and gastric cardia cancer in a nationwide study in Sweden. Eur J Cancer 2008;44:1566–71.
- [59] Thrift AP, Nagle CM, Fahey PP, Russell A, Smithers BM, Watson DI, et al. The influence of prediagnostic demographic and lifestyle factors on esophageal squamous cell carcinoma survival. Int J Cancer 2012;131:759–68.
- [60] Thrift AP, Nagle CM, Fahey PP, Smithers BM, Watson DI, Whiteman DC. Predictors of survival among patients diagnosed with adenocarcinoma of the esophagus and gastroesophageal junction. Cancer Causes Control 2012;23:555–64.
- [61] Trivers KF, Roos AJDE, Gammon MD, Vaughan TL, Risch HA, Olshan AF, et al. Demographic

and Lifestyle Predictors of Survival in Patients with Esophageal or Gastric Cancers
2005;3565:225–30.

- [62] Wang N, Tan B, Cao F, Song Q, Wang J, Jia Y, et al. Prognostic influence of smoking on esophageal squamous cell carcinoma. Int J Clin Exp Med 2015;8:18867–72.
- [63] Zhang SS, Yang H, Luo KJ, Huang QY, Chen JY, Yang F, et al. The impact of body mass index on complication and survival in resected oesophageal cancer: a clinical-based cohort and meta-analysis. Br J Cancer 2013;109:2894–903.
- [64] Zhang F, Han H, Wang C, Wang J, Zhang G, Cao F. A retrospective study: The prognostic value of anemia, smoking and drinking in esophageal squamous cell carcinoma with primary radiotherapy. World J Surg Oncol 2013;11:no pagination.
- [65] Zhang D, Zhou X, Bao W, Chen Y, Cheng L, Qiu G, et al. Plasma fibrinogen levels are correlated with postoperative distant metastasis and prognosis in esophageal squamous cell carcinoma. Oncotarget 2015;6:38410–20.
- [66] Fahey PP, Mallitt K-A, Astell-Burt T, Stone G, Whiteman DC. Impact of pre-diagnosis behavior on risk of death from esophageal cancer: a systematic review and meta-analysis. Cancer Causes Control 2015;26:1365–73.
- [67] Arnold M, Soerjomataram I, Ferlay J, Forman D. Global incidence of oesophageal cancer by histological subtype in 2012. Gut 2015;64:381–7.
- [68] Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87–108.
- [69] Wu I-C, Wu C-C, Lu C-Y, Hsu W-H, Wu M-C, Lee J-Y, et al. Substance use (alcohol, areca nut and cigarette) is associated with poor prognosis of esophageal squamous cell carcinoma. PLoS One 2013;8:e55834.

- [70] Hurmuzlu M, Øvrebø K, Monge OR, Smaaland R, Wentzel-Larsen T, Viste A. High-dose chemoradiotherapy followed by surgery versus surgery alone in esophageal cancer: a retrospective cohort study. World J Surg Oncol 2010;8:46.
- [71] Ji W, Zheng W, Li B, Cao C, Mao W. Influence of body mass index on the long-term outcomes of patients with esophageal squamous cell carcinoma who underwent esophagectomy as a primary treatment: A 10-year medical experience. Medicine (Baltimore) 2016;95:e4204.
- [72] Huang Q, Luo K, Yang H, Wen J, Zhang S, Li J, et al. Impact of alcohol consumption on survival in patients with esophageal carcinoma: A large cohort with long-term follow-up. Cancer Sci 2014;105:1638–46.
- [73] Ferronha I, Castro C, Carreira H, Bento MJ, Carvalho I, Peleteiro B, et al. Prediagnosis lifestyle exposures and survival of gastric cancer patients: a cohort study from Portugal. Br J Cancer 2012;107:537–43.
- [74] Gong EJ, Ahn JY, Jung HY, Lim H, Choi KS, Lee JH, et al. Risk factors and clinical outcomes of gastric cancer identified by screening endoscopy: A case-control study. J Gastroenterol Hepatol 2014;29:301–9.
- [75] Han MA, Kim Y-W, Choi IJ, Oh MG, Kim CG, Lee JY, et al. Association of smoking history with cancer recurrence and survival in stage III-IV male gastric cancer patients. Cancer Epidemiol Biomarkers Prev 2013;22:1805–12.
- [76] Huang X-E, Tajima K, Hamajima N, Kodera Y, Yamamura Y, Xiang J, et al. Effects of Dietary, Drinking, and Smoking Habits on the Prognosis of Gastric Cancer. Nutr Cancer 2000;38:30–6.
- [77] Posteraro B, Persiani R, Dall’Armi V, Biondi A, Arzani D, Sicoli F, et al. Prognostic factors and outcomes in Italian patients undergoing curative gastric cancer surgery. Eur J Surg Oncol 2014;40:345–51.
- [78] Smyth EC, Capanu M, Janjigian YY, Kelsen DK, Coit D, Strong VE, et al. Tobacco Use Is

Associated with Increased Recurrence and Death from Gastric Cancer. Ann Surg Oncol 2012;19:2088–94.

- [79] Kai K, Koga H, Aishima S, Kawaguchi A, Yamaji K, Ide T, et al. Impact of smoking habit on surgical outcomes in non-B non-C patients with curative resection for hepatocellular carcinoma. World J Gastroenterol 2017;23:1397–405.
- [80] Kolly P, Knopfli M, Dufour J-F. Effect of Smoking on Survival of Patients with Hepatocellular Carcinoma. Liver Int 2017:1–6.
- [81] Shih WL, Chang HC, Liaw YF, Lin SM, Lee SD, Chen PJ, et al. Influences of tobacco and alcohol use on hepatocellular carcinoma survival. Int J Cancer 2012;131:2612–21.
- [82] Abe H, Aida Y, Ishiguro H, Yoshizawa K, Miyazaki T, Itagaki M, et al. Alcohol, postprandial plasma glucose, and prognosis of hepatocellular carcinoma. World J Gastroenterol 2013;19:78–85.
- [83] Akahoshi H, Taura N, Ichikawa T, Miyaaki H, Akiyama M, Miura S, et al. Differences in prognostic factors according to viral status in patients with hepatocellular carcinoma. Oncol Rep 2010;23:1317–23.
- [84] Borzio M, Colloredo G, Pioltelli P, Quagliuolo M. Epidemiology and outcome of hepatocellular carcinoma in Lombardy. Dig Liver Dis 2007;39:1011–7.
- [85] Hosokawa T, Kurosaki M, Tsuchiya K, Matsuda S, Muraoka M, Suzuki Y, et al. Hyperglycemia is a significant prognostic factor of hepatocellular carcinoma after curative therapy. World J Gastroenterol 2013;19:249–57.
- [86] Siegel AB, Goyal A, Salomao M, Wang S, Lee V, Hsu C, et al. Serum adiponectin is associated with worsened overall survival in a prospective cohort of hepatocellular carcinoma patients. Oncology 2015;88:57–68.

- [87] Uyeturk U, Kos FT, Helvaci K, Sonmez OU, Turker I, Aktas G, et al. Demographic features and factors affecting overall survival in patients with hepatocellular carcinoma: A retrospective analysis in Turkey 2013;29:617–23.
- [88] Ganti AK, Potti A, Koch M, Tendulkar K, Hanekom D, Koka V, et al. Predictive value of clinical features at initial presentation in pancreatic adenocarcinoma: a series of 308 cases. Med Oncol 2002;19:233–7.
- [89] Zell JA, Rhee JM, Ziogas A, Lipkin SM, Anton-Culver H. Race, Socioeconomic Status, Treatment, and Survival Time among Pancreatic Cancer Cases in California. Cancer Epidemiol Biomarkers Prev 2007;16 :546–52.
- [90] Olson SH, Chou JF, Ludwig E, O'Reilly E, Allen PJ, Jarnagin WR, et al. Allergies, obesity, other risk factors and survival from pancreatic cancer. Int J Cancer 2010;127:2412–9.
- [91] Dandona M, Linehan D, Hawkins W, Strasberg S, Gao F, Wang-Gillam A. Influence of obesity and other risk factors on survival outcomes in patients undergoing pancreaticoduodenectomy for pancreatic cancer. Pancreas 2011;40:931–7.
- [92] Gong Z, Holly EA, Bracci PM. Obesity and survival in population-based patients with pancreatic cancer in the San Francisco Bay Area. Cancer Causes Control 2012;23:1929–37.
- [93] Wang D, Wang Z, Zhang L, Qiu M, Luo H, Ren C, et al. Are risk factors associated with outcomes in pancreatic cancer? PLoS One 2012;7:e41984.
- [94] Lakatos G, Balázs A, Kui B, Gódi S, Szücs Á, Szentesi A, et al. Pancreatic Cancer: Multicenter Prospective Data Collection and Analysis by the Hungarian Pancreatic Study Group. J Gastrointest Liver Dis 2016;25:219–25.
- [95] Delitto D, Zhang D, Han S, Black BS, Knowlton AE, Vlada AC, et al. Nicotine Reduces Survival via Augmentation of Paracrine HGF–MET Signaling in the Pancreatic Cancer Microenvironment. Clin Cancer Res 2016;22.

- [96] Pelucchi C, Galeone C, Polesel J, Manzari M, Zucchetto A, Talamini R, et al. Smoking and body mass index and survival in pancreatic cancer patients. Pancreas 2014;43:47–52.

Table 1. Pooled results from random effects meta-analysis for the association between smoking, alcohol consumption and overall survival in GI cancer patients

	Colorectal cancer			Oesophageal cancer			OSCC			OAC			Gastric cancer			Pancreatic cancer		
	n	Pooled HR (95% CI)	I ² (%)	n	Pooled HR (95% CI)	I ² (%)	n	Pooled HR (95% CI)	I ² (%)	n	Pooled HR (95% CI)	I ² (%)	n	Pooled HR (95% CI)	I ² (%)	n	Pooled HR (95% CI)	I ² (%)
<u>Smoking</u>																		
Ever	4	1.42 (1.29-1.56)	0	10	1.07 (0.94-1.21)	30	8	1.07 (0.86-1.32)	34	1			6	1.25 (1.02-1.55)	6	5	1.20 (1.05-1.37)	56
Current	11	1.39 (1.21-1.60)	73	5	1.12 (0.91-1.39)	0	2	1.41 (0.96-2.09)	0	2	0.99 (0.73-1.36)	0	6	1.39 (0.96-2.01)	82	5	1.19 (0.97-1.46)	49
Former	9	1.10 (0.96-1.27)	67	5	0.97 (0.78-1.20)	19	2	1.44 (0.81-2.55)	47	2	0.88 (0.68-1.14)	0	5	1.05 (0.76-1.45)	71	5	1.14 (1.01-1.30)	16
Light	5	1.13 (0.88-1.45)	51	3	1.09 (0.73-1.65)	53	2	1.46 (1.05-2.03)	0	1			6	1.29 (0.89-1.86)	81	0		
Moderate				5	1.29 (0.87-1.90)*	67	2	1.33 (0.75-2.35)*	61	1			6	1.13 (0.81-1.58)	76	0		
Heavy	5	1.52 (1.31-1.77)	7	3	1.27 (0.98-1.66)*	16	2	1.46 (1.05-2.03)*	0	1			2	1.97 (1.08-3.59)	55	0		
Recent former	4	1.40 (1.22-1.61)	0	0			0			0			0			2	1.42 (1.16, 1.74)	0
Long former	4	1.18 (1.01-1.39)	12	0			0			0			0			2	1.11 (0.85, 1.44)	37
<u>Alcohol</u>																		
Ever	3	1.83 (0.66-5.04)	89	8	1.23 (1.10-1.37)	34	5	1.36 (1.07-1.74)	55	1			3	1.09 (0.94-1.26)	61	1		
Light	7	0.85 (0.77-0.94)	45	5	1.00 (0.78-1.28)	34	2	0.99 (0.29-3.35)	82	2	0.99 (0.70-1.39)	0	5	1.03 (0.87-1.22)	22			
Moderate	3	0.89 (0.72-1.11)	35	4	1.26 (0.92-1.73)	59*	2	1.09 (0.25-4.67)*	88	2	1.34 (0.95-1.89)*	0	3	0.95 (0.71-1.28)*	6	1		
Heavy	6	0.92 (0.84-1.01)	0	7	1.23 (0.94-1.61)	62*	3	1.04 (0.54-2.01)*	78	2	1.01 (0.70-1.47)*	0	5	1.08 (0.95-1.23)*	0	1		

* Comparison to light/never smokers or light/non-drinkers. All other comparisons are to never smokers or non-drinkers.

Insufficient studies for meta-analyses of liver cancer

Abbreviations: n: number of studies; OAC: Oesophageal adenocarcinoma; OSCC: Oesophageal squamous cell carcinoma.

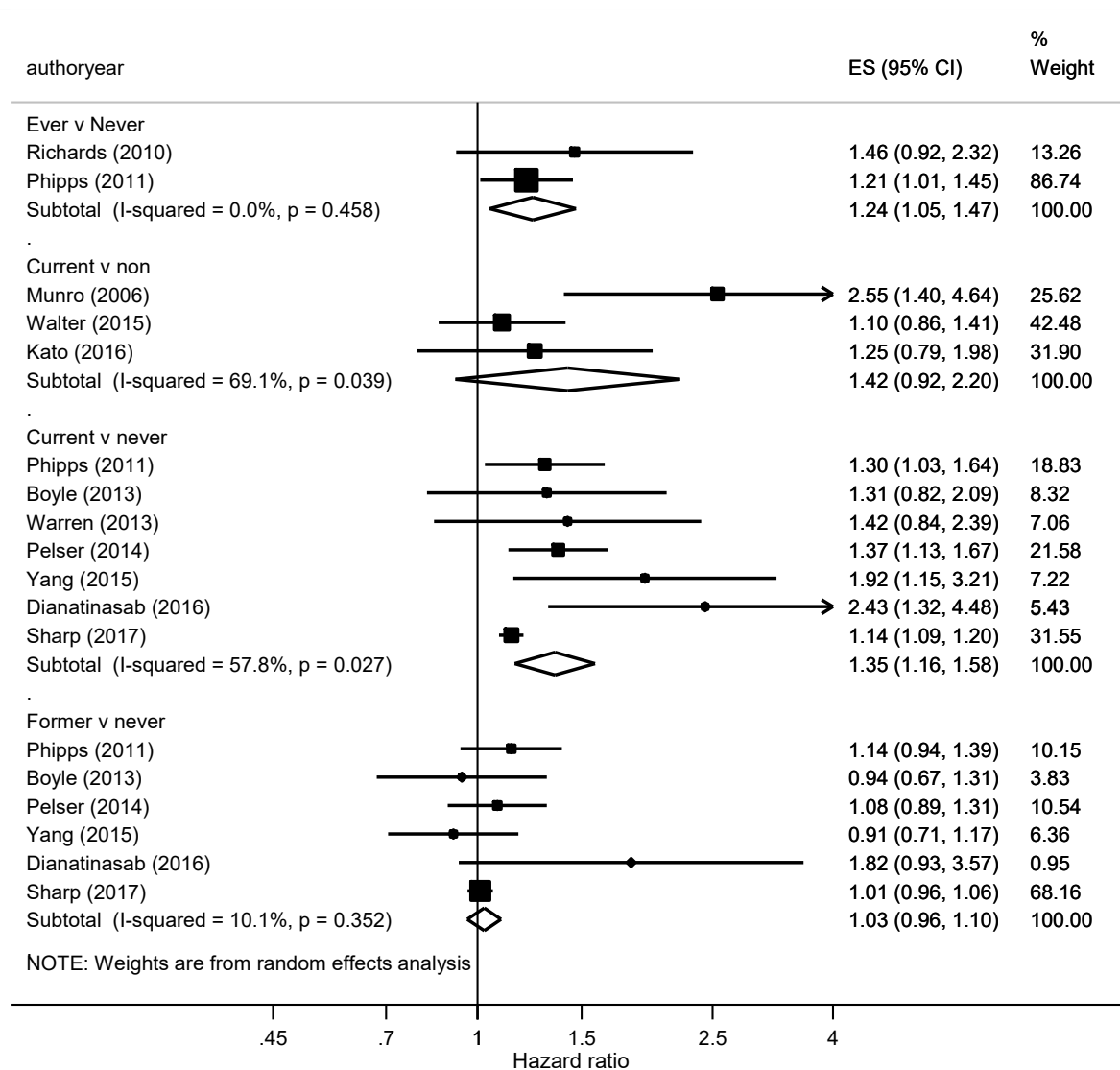


Figure 1. Random effects meta-analysis between smoking status and cancer specific survival in colorectal cancer patients.

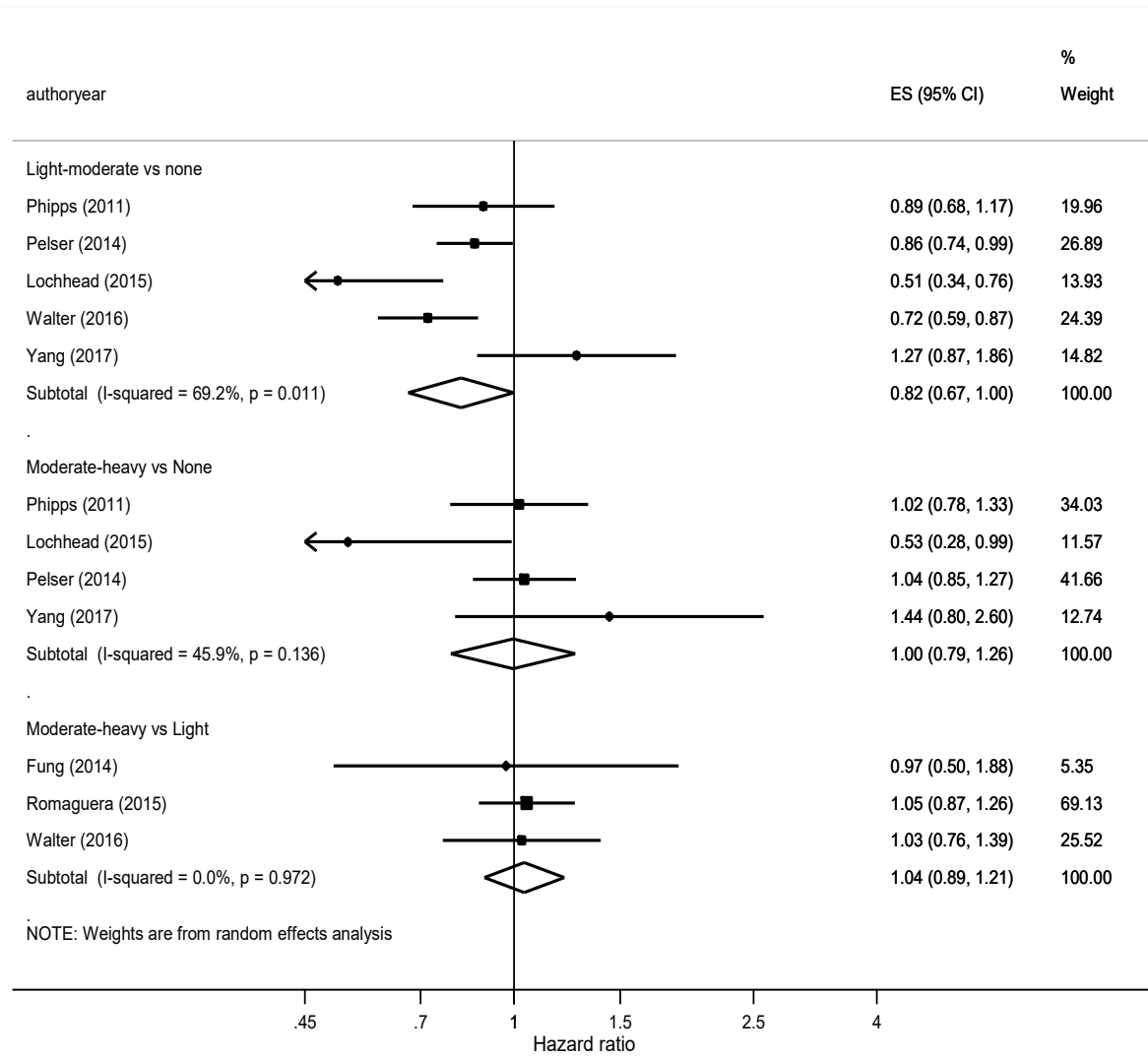


Figure 2. Random effects meta-analysis between alcohol consumption and cancer specific survival in colorectal cancer patients.

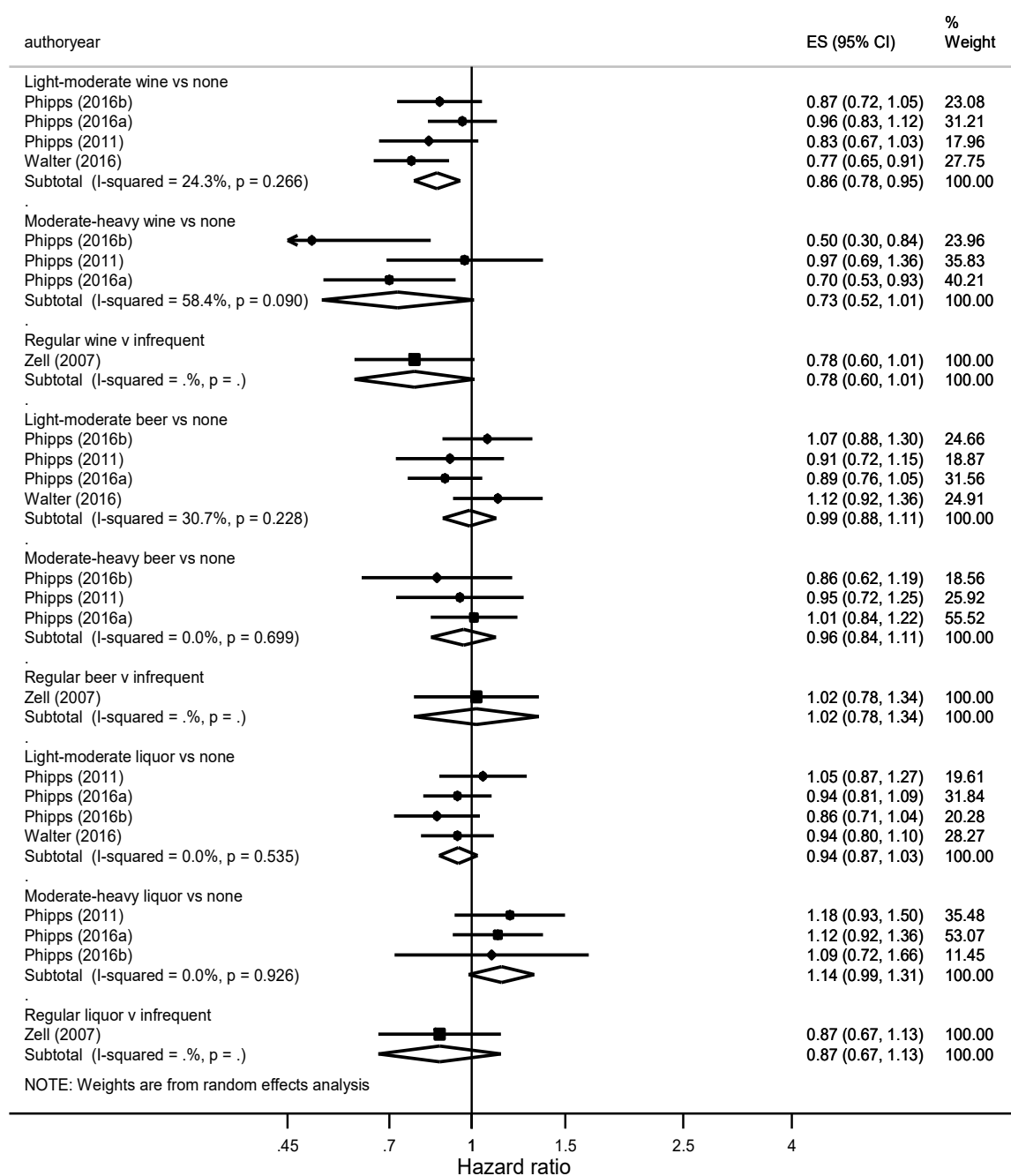


Figure 3. Random effects meta-analysis between type of alcohol consumption and overall survival in colorectal cancer patients.